Arginase Deficiency

Lauren Ballard, Alex Belardo, Lainie Boyle, Abby Dryden, Rachel Kirchner, M'Lynn Gwinner, Shreya Nalluri, & Julia Slogar

THE OHIO STATE UNIVERSITY

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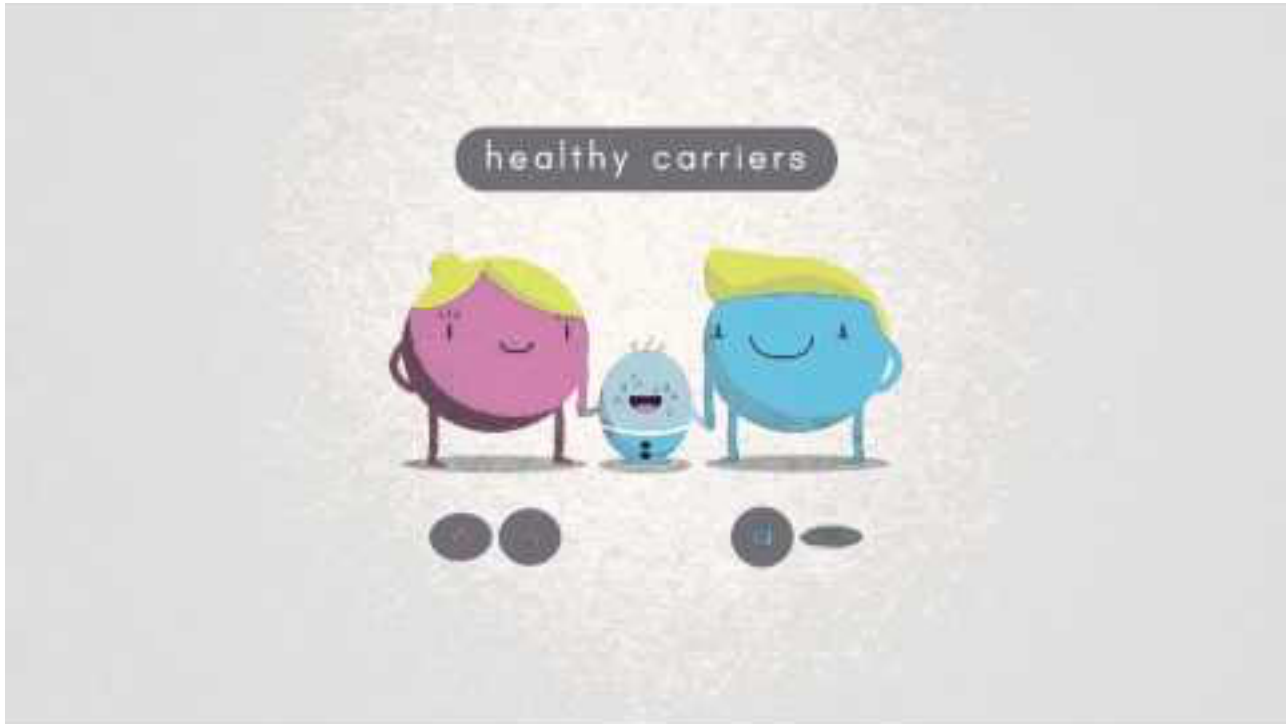
Argininemia: An autosomal recessive disorder

Video on Inheritance Patterns



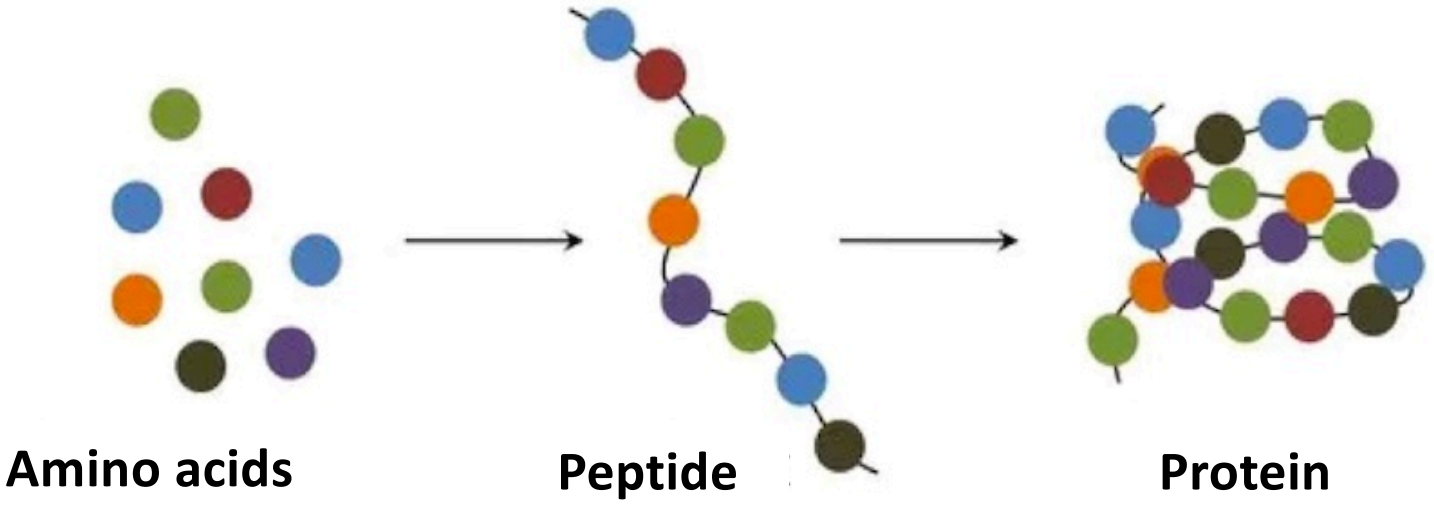
HNEkidshealth. “Autosomal Recessive Inheritance - Genetics.” YouTube, YouTube, 30 Mar. 2015, www.youtube.com/watch?v=Nv6qUsKYodA.

Argininemia

- Inherited disorder that causes arginine (amino acid) and ammonia to build up in the blood
- The deficiency usually becomes evident by 3 years of age
- Occurs once in every 300,000 to 1,000,000 individuals
- Caused by a mutation in the *ARG1* gene, which encodes the enzyme arginase
- Inherited in an autosomal recessive pattern

Baby's first foods: Where to begin? Digital image retrieved October 31, 2018 from https://www.kabritausa.com/blog/babys-first-foods-begin/

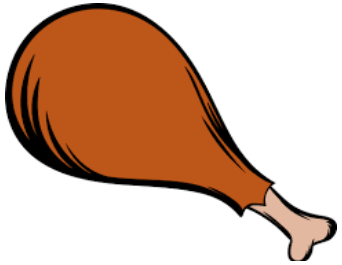
Protein Metabolism



How Your Body Uses Amino Acids as Proteins. Digital image retrieved October 31, 2018 https://socratic.org/questions/amino-acids-as-monomers-of-protein

- Amino Acids are the building blocks of proteins
- Dietary protein must be broken down into amino acids

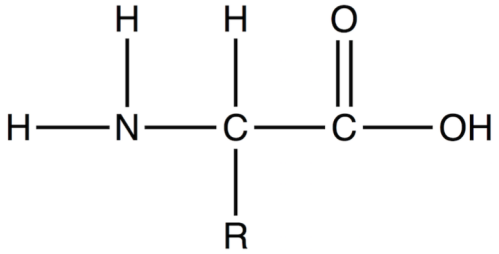
Protein Metabolism



Dietary Protein

NH_4^+

Urea (waste)



Amino Acids

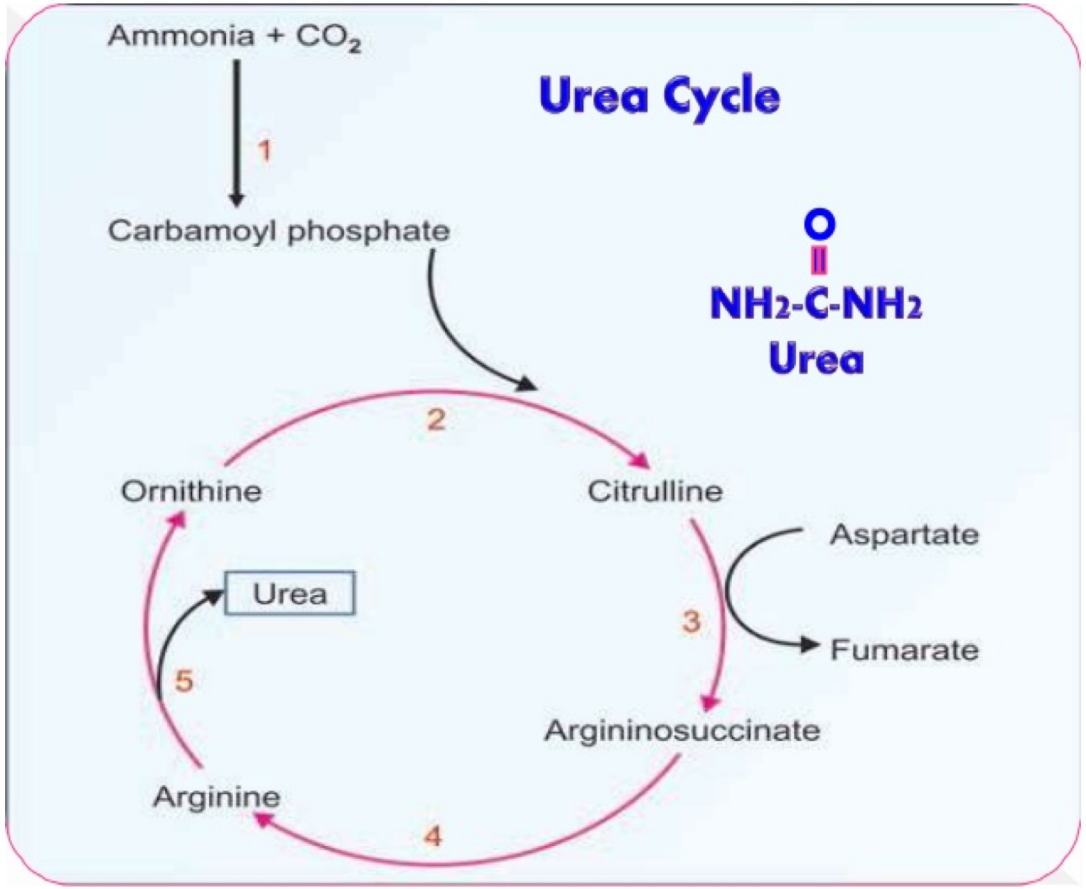
Intracellular Protein

Carbon backbone

Glucose (energy)

Argininemia and the Urea Cycle

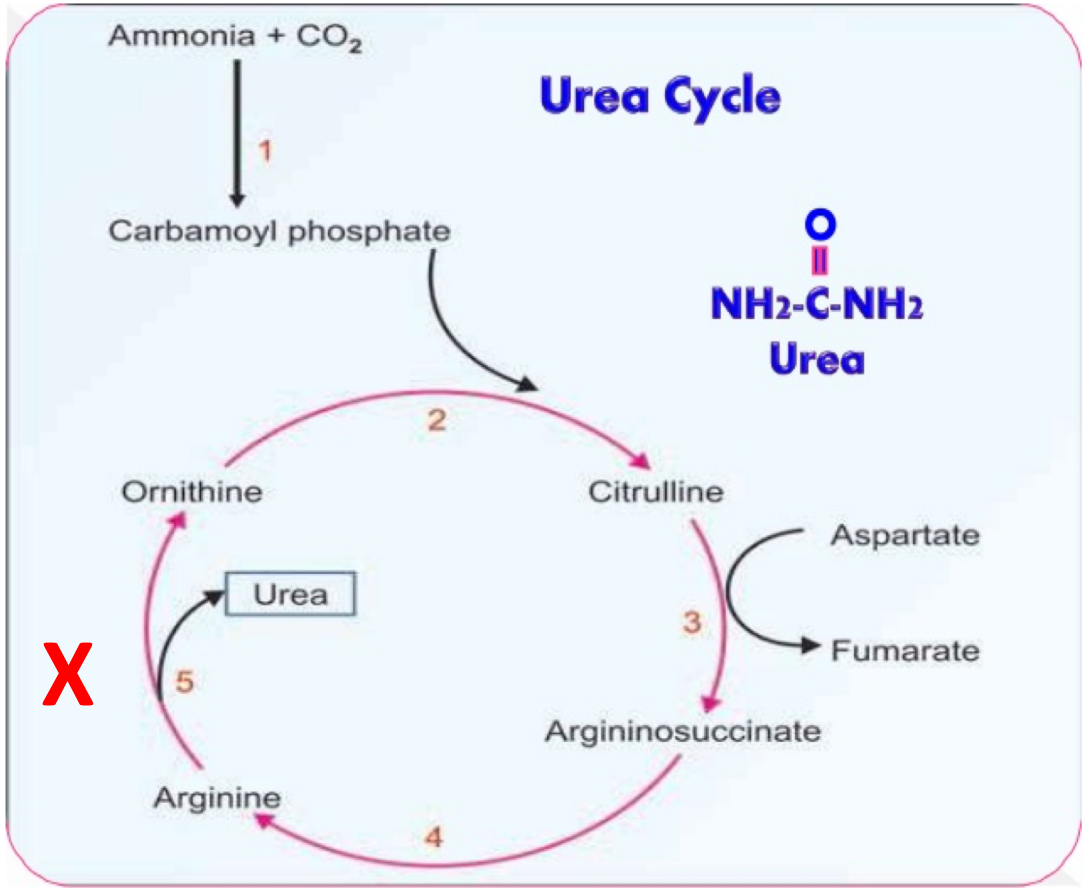
- Disorder of the **urea cycle**
- Our bodies produce ammonia as metabolic waste
  - Ammonia is highly toxic and must be discarded
- The urea cycle in the liver converts ammonia to urea, a less toxic compound



Urea Cycle. Digital image retrieved October 31, 2018 from https://www.slideshare.net/YESANNA/urea-cycle-44200147

What is Argininemia?

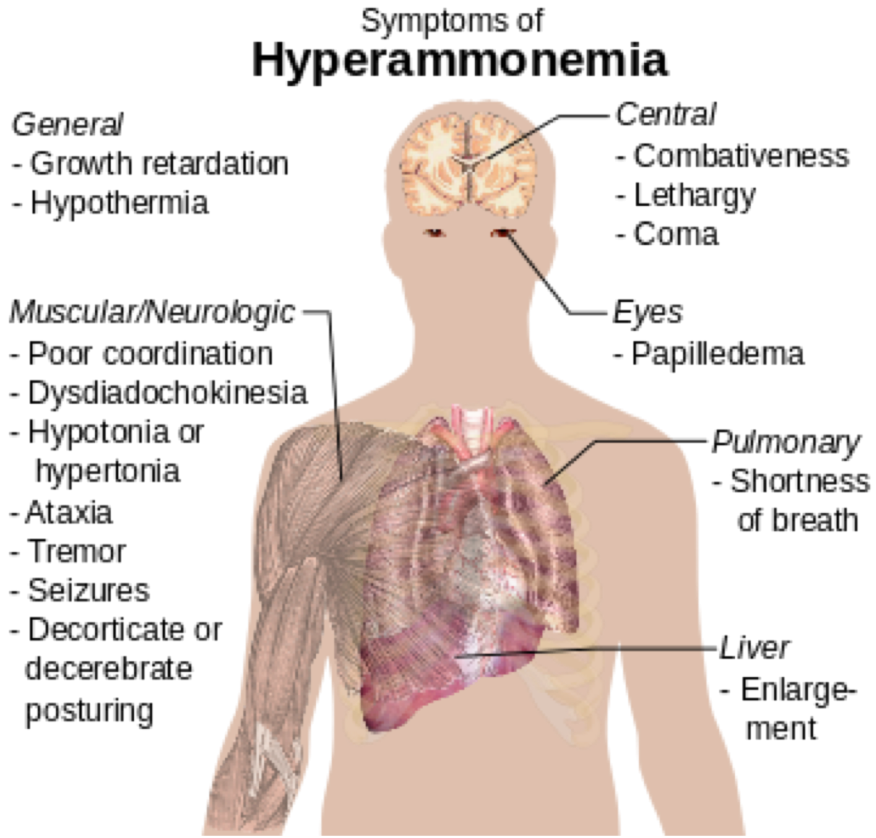
- Disorder of the **urea cycle**
- Dysfunctional arginase enzyme disrupts final step of urea cycle
- Build-up of ammonia in the blood



Urea Cycle. Digital image retrieved October 31, 2018 from https://www.slideshare.net/YESANNA/urea-cycle-44200147

Ammonia Toxicity

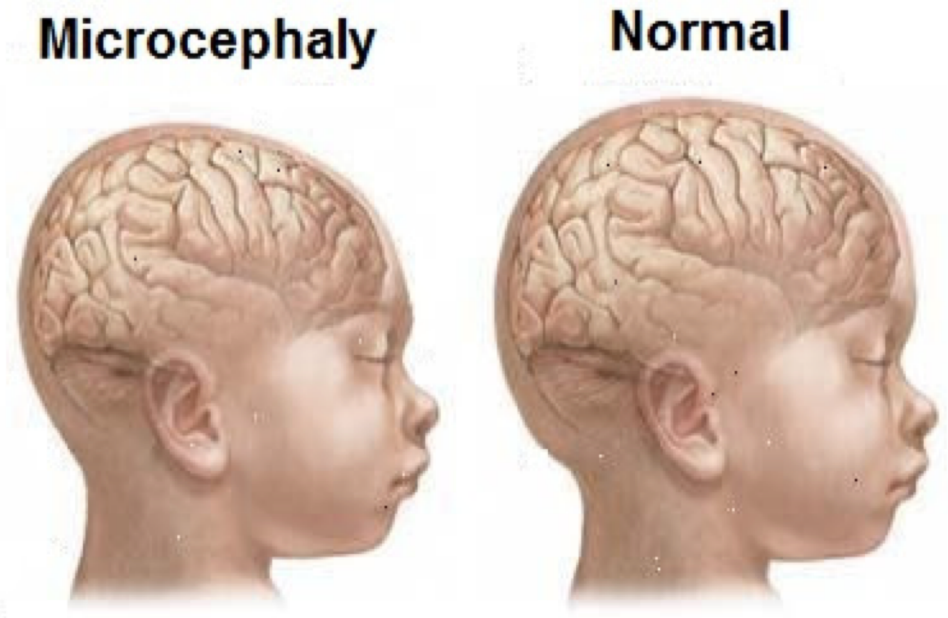
- Generation of cellular energy is dampened
- Ammonia build-up indirectly results in accumulation of water (cerebral edema)
- Neurotransmission is adversely affected



Symptoms of Hyperammonemia. Digital image retrieved October 31, 2018 from https://ru.m.wikipedia.org/wiki/%D0%A4%D0%B0%D0%B9%D0%BB:Symptoms_of_hyperammonemia.svg

Symptoms

- Poor growth (present in all)
- Stiff muscles and increased reflexes (spasticity)
- Developmental delay
- Intellectual disability
- Seizures
- Microcephaly
- Problems with balance and coordination



Leads to cognitive/neurological impairment

HOW SMALL DOES THE HEAD HAVE TO BE TO QUALIFY AS MICROCEPHALY? Digital image retrieved October 31, 2018 form http://www.medfriendly.com/microcephaly.html

Neonatal diagnosis

Texas Newborn Screening - Info for Parents. Digital image retrieved October 31, 2018 from https://www.dshs.texas.gov/newborn/expandparent.shtm

- Blood tests to determine the levels of arginine and ammonia
- Genetic testing can identify if a child has a mutation in the ARG1 gene

Prognosis

Disease Trajectory

- Most of those affected (75%) live long lives; diet and supplements can allow for a relatively unimpaired life

Severity

- Depends on degree of enzymatic deficiency
- Prevention of primary symptoms reduces intellectual impairment
- Ability to follow diet and medication regimen lessens symptom severity

Prognosis

Lack of attention can result in:

- severe intellectual impairment
- loss of the ability to walk
- loss of bladder and bowel control

If diagnosed and treated properly:

- mild to moderate intellectual impairment
- seizures
- muscle stiffness

Therapy and treatment

- Dietary restriction of arginine or general restriction of protein
  - Cannot entirely eliminate protein from the diet
- Benzoates to promote amino acid excretion, lowering ammonia levels
- Seizures caused by argininemia can be treated with medication
- Liver transplantation if blood ammonia levels cannot be controlled

MyFItnessPal. Image retrieved October 31, 2018 from https://www.dshs.texas.gov/newborn/expandparent.shtm

Overcoming Argininemia – a real life story

Jackson Fukuda

- As a toddler, showed issues with coordination
- Began to cough and vomit after the smallest bit of exercise
- At age 5, weighed only 25 lbs
- Underwent constant therapy and treatment into adulthood
- Founded an organization called National Urea Cycle Disorder Foundation (NUCDF)

Support Groups

- National Urea Cycle Disorders Foundation (NUCDF)
  - Part of National Organization of Rare Disorders
  - Helps connect families to information, specialists and other families going through similar experiences

- Urea Cycle Disorders Consortium (UCDC)
  - Part of the Rare Diseases Clinical Research Network
  - Helps inform the public of new clinical research and provides ways to get involved with new clinical trials

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Arginase Deficiency – Project Team

Student	Project Role
Rachel Kirchner (Text)	Urea Cycle
M'Lynn Gwinner (Illustration)	Symptoms
Abby Dryden	Diagnosis
Alex Belardo	Story
Julia Sloger	Biochemical Features
Lainie Boyle	Treatment
Lauren Ballard	Background
Shreya Nalluri	Prognosis

Sources

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